REMARKS/ARGUMENTS

Claims 18-24 and 38 are pending. Claim 18 has been amended. Claims 25-37 have been withdrawn.

All claims were rejected over Chou (WO 98/05379) because it was considered obvious to modify the apparatus of Chou by determining if a time delay value exceeds and/or is less than a preceding value average. It was considered known in the art to provide predictable results pertaining to utilizing a threshold setting used for only obtaining optimal pulses measured by a sensor so as to calculate an adjustable time delay responsive from the pulse in order to provide a burst of stimulation energy at any desired point during each heart beat cycle.

The present invention as defined by independent claim 18 relates to a method of treating a mammal or other living organism having a heart and a peripheral vascular system, in particular a human being, to achieve a heart load reduction.

The claimed invention is based on the wholly surprising discovery that it is possible to secure an optimized reduction in a patient's pulse rate and thereby achieve a highly significant net reduction in the heart load by using a non-invasive method in synchronization with the heart rhythm in the counterpulsation mode. This is a particularly surprising discovery because it is not at all evident that a totally non-invasive stimulation of, for example, a leg muscle, on only one of the many peripheral branches of the cardiovascular tree, would ever be able to increase coronary blood flow and reduce the heart load by a significant amount. Indeed it is totally surprising that the degree of reduction of the heart load achieved in these tests is similar to that achieved with the risky, fully invasive, extra-aortal muscular flap wrapped around the aorta assisted by electrostimulation.

More specifically it was found that, by correctly setting pressure pulsations for the individual patient, a type of resonant phenomena arises which could be exploited, so that a small perturbation of the peripheral vascular system leads to an optimized reduction in the pulse rate and through this a net reduction in the heart load. It is particularly favorable that the reduction in the pulse rate is also accompanied by a reduction in the systolic pressure so that a very

pronounced effect with respect to the heart load is achieved by just a small perturbation of only one peripheral branch of the cardiovascular tree.

The claimed invention therefore provides an almost universally applicable method and apparatus by which a substantial degree of heart unloading can be achieved by appropriate stimulation of the patient which can be applied without practical time limitation and in particular without any restrictions of the muscles to be stimulated, with the exception of the heart muscle itself.

This is achieved with an electrotherapy apparatus having a sensor for detecting periodically recurring signal peaks, for example the R-R peaks of an electrocardiogram of a person, a processor for deriving from the periodically recurring signal peaks of the ECG, a time delay corresponding to approximately the end of the T-wave, a trigger system or a circuit initiated by an output signal of the processor or embodied within the processor for applying electrical stimulations to one or more active electrodes provided on the person at a time related to the end of the time delay, with the processor also being adapted to carry out comparisons between individual heart beat spectra detected by the ECG using steps (a) to (n) of claim 1. Such a comparison is necessary, because the heart rate of patients is not constant; i.e. it fluctuates during treatment, for example, because the patient starts to relax during the treatment, which causes the heart rate to generally slow down, and a human's heart beat is also generally subjected to heart rate minor fluctuations even when the patient is at complete rest.

The present invention recognizes that, to achieve a reduction in heart load, the electrical stimulation has to take place starting at around the end of the T-wave, i.e. in synchronization with the heart rhythm in the counterpulsation mode, and continuing for a period that finishes before the next R-peak. Having made this recognition, applicants provide the electrotherapy apparatus with a processor which is capable of comparing the recurring heart signals of the patient, detected using the ECG, to a stimulation pattern designed for that patient. Moreover, the processor is capable of subsequently adapting the stimulation pattern when the heart rate changes. In particular, the time delay between the R-wave and the end of the T-wave has to be re-adjusted for each pulse, using the so-called Bazett relationship.

Steps (a) to (n) of claim 18 are performed by the processor and achieve such a readjustment. The recited steps set forth how the processor processes the signals of successively detected signal peaks which correspond to a person's heart rate. The processor thereby obtains certain values from the detected signal peaks, such as, for example, the offset between the R-peak and the T-wave, and/or the duration of individual R-R phases, etc.

More specifically, in accordance with step (a) of claim 18, the processor determines the time between successive pairs of signal peaks, such as the R-R peaks, and thus determines the person's heart rate. In step (b) the processor compares the value acquired for the heart rate with maximum and minimum permissible technical limits permitted by the apparatus, and/or in step (c) the processor compares the value of the heart rate with maximum and minimum permissible selected limits.

In step (d) the processor determines whether the value for the heart rate exceeds a preceding value or a preceding value averaged over a plurality of heart beats by more than a defined amount, and in step (e) the processor determines whether the value is less than a preceding value or a preceding value averaged over a plurality of heart beats by more than a defined amount. In step (f) the processor initiates the trigger system or circuit only when the comparisons of steps (b) and/or (c) are favorable and the determinations made in steps (d) and (e) show that the value does not exceed or undercut the preceding value or the preceding average value by more than the defined amount.

In step (g) the processor closes a measurement window for the sensor once it has been determined that the comparisons made in steps (b) and/or (c) are favorable and that the values determined in steps (d) and (e) show that the value for the detected heart beat does not exceed the preceding value or the preceding average value by more than the defined amount and that that value is not less than the preceding value or the preceding average value by more than the defined amount. The processor is configured so that the measurement window has to be closed prior to triggering the trigger system.

In addition to this time delay, the processor calculates a maximum stimulation length in step (h). In step (i) the processor checks that the derived value of the time delay is greater than or equal to a delay time which is equivalent to a trigger delay plus a calculation

delay, where the trigger delay is the delay between the initiation of a trigger signal delivered by the sensor which corresponds to the detection of a first signal peak and the time this signal takes to reach the processor and where the calculation delay is the time required by the processor to derive the delay.

Step (j) checks that the derived time delay is less than or equal to the maximum stimulation length and, if necessary, revises the derived time delay, such that it fulfils the two conditions of step (j) that the derived time delay is greater than or equal to the trigger delay plus the calculation delay and that the derived time delay is less than or equal to the maximum stimulation length.

Step (k) of claim 18 calculates a maximum duration which is equal to the maximum stimulation length minus the time delay, and in step (l) the processor calculates a duration of the electrical stimulation and a maximum duration value which is equal to the maximum stimulation length minus the derived time delay. Following this the processor checks whether the calculated duration is less than or equal to the maximum duration and if not adapts the duration such that it is less than or equal to the maximum duration.

In step (m), an open measurement window time is calculated which is equal to the derived time delay, or the adapted delay, if the delay was adapted, plus the duration or the adapted duration, if the duration was adapted, plus a safety margin. Finally in step (n) the processor sends an output signal to the trigger system during the measurement window and opens the measurement window at the calculated time permitting the recognition of the detection of a further peak of the electrocardiogram by the sensor.

Thus, the processor of the present invention defined by claim 18 is not only adapted to apply electrical stimulation to one or more active electrodes, it also controls the stimulation so that the stimulation is provided relative to the end of the T-wave for a duration which does not exceed technical and/or harmful limits for the patient's heart.

Chou, over which all claims, including independent claim 18, were rejected, teaches to stimulate a human body with reoccurring bursts of energy. The stimulating mechanism includes a sensing mechanism for synchronizing the stimulation with the heart beat

of the human body by causing energy bursts to occur at the same rate as the heart beat of the human body. As disclosed on page 1, lines 23-25 of Chou, Chou is particularly useful in reducing the pain and discomfort caused by various human ailments such as headaches, arthritis, rheumatism, back pain and drug and alcohol withdrawal symptoms and is not intended, as is true for the present invention defined by claim 18, to help in the treatment of heart load problems.

Fig. 4 of Chou discloses a portion of an electrocardiogram showing various phases of a heart beat cycle; in particular it shows a QRSTP diagram of the human heart and indicates the systole and diastole phases of the human heart. The only reference in Chou to the T-wave of the human heart is the indication of its position in Fig. 4.

As persons of ordinary skill in the art know, many treatments have been proposed and used in the prior art which affect the cardiovascular system of human beings. Well known among such systems are cardiosynchronized electrophysiological methods and apparatus, which comprise methods by which the heart pulse rate is predetermined by means of a sensor and stimulation is delivered in a rhythm at any time within the heart cycle and is synchronized in some way with the heart cycle. Such cardiosynchronized methods and apparatus can be subdivided into two classes, namely the <u>simpulsation mode</u> and the <u>counterpulsation mode</u>. Chou is concerned exclusively with the <u>simpulsation mode</u>, whereas the present invention is concerned exclusively with the <u>counterpulsation mode</u>.

In the <u>simpulsation mode</u> of a cardiosynchronized electrostimulation of muscles disclosed by Chou, the electric impulses are synchronized with the heart pulse rate so that the heart and the stimulated muscle are contracting at the same time; i.e. in the systole phase the heart is contracting and the stimulated muscle is contracting, in the diastole phase the heart is relaxing and the muscle is relaxing.

In the <u>counterpulsation mode</u> of a cardiosynchronized electrostimulation of muscles of the present invention defined by claim 18, the electric impulses are timed in such a way, relative to the heart pulse rate, that the heart and the stimulated muscle are contracting in opposition to each other; i.e. in the systole phase the heart is contracting and the stimulated muscle is relaxing, in the diastole phase the heart is relaxing and the stimulated muscle is contracting.

The cardiosynchronized electrophysiological methods using the simpulsation mode do not result in a significant change of the heart load when compared to the heart load of the same person without that person being subjected to stimulation. A person of ordinary skill in the art will recognize from Fig. 4 of Chou that Chou stimulates the patient using the simpulsation mode and not, as is the case in the present invention, the counterpulsation mode.

This is clear because Chou does not provide electrical stimulation to the human heart in a region around the end of the T-wave. Thus, Chou essentially discloses a prior art device as is discussed on pages 4-8 of WO 01/13990 A1. Chou does not teach or in any manner suggest to a person of ordinary skill in the art that counterpulsation is possible, nor does Chou teach or suggest that one can use the Bazett relationship to calculate the position of the T-wave relative to the R-peak in a patient's heart rate spectrum.

Moreover, considering the synchronizing mechanism of Chou which is adapted to produce energy bursts using a stimulating mechanism that stimulates at the same rate or frequency as the human heart beat, the heart beat being detected by the sensing mechanism, Chou teaches in relevant parts that:

"*This apparatus includes a stimulating mechanism for stimulating a living human body 10 with reoccurring bursts of energy* " (page 4, lines 14-15 of Chou).

"*The apparatus of the present invention further includes a sensing mechanism for sensing the heartbeat of the human body 10. In the embodiment of FIG. 1, this sensing mechanism includes a heart activity sensor 18 adapted to detect the cyclic activity of the human heart and detector circuitry 20 coupled to the heart activity sensor 18 for detecting the occurrence of unique points in the heartbeat cycles. The heart activity sensor 18 may include electrocardiogram (ECG) electrodes adapted to be attached to the human body 10 for sensing the electrical currents produced by the activity of the heart*" (page 6, lines 20-26).

"*When the sensing mechanism uses electrocardiogram electrodes, detector circuitry 20 detects the occurrence of the R wave peaks of the ECG signal* "(page 7, lines 9-10).

"*The embodiment of FIG. 1 further includes a synchronizing mechanism coupled to the stimulating mechanism and to the sensing mechanism for synchronizing the body*

stimulation with the heartbeat by causing the energy bursts produced by the stimulating mechanism to occur at the same rate or frequency as the human heartbeat detected by the sensing mechanism. This synchronizing mechanism includes circuitry for producing reoccurring control signal bursts for controlling the activation of the stimulating mechanism, time delay circuitry 27 for determining the position of the control signal bursts relative to the detector output pulses and time duration circuitry 28 for determining the time duration of the control signal bursts" (page 7, lines 14-22).

Thus Chou detects the heart rate of a patient; i.e. Chou performs step (a) of claim 18 of the present application. However, Chou does not compare the detected heart rate to either maximum or minimum technical or predetermined limits as is the case in steps (b) and (c) of claim 18 and, importantly, Chou does not perform step (a) using a processor. Consequently steps (d) to (g) of claim 18 are also not carried out by Chou. Moreover, there is no motivation or teaching in Chou which would lead a person of ordinary skill in the art to modify the apparatus in Chou in such a manner that he would be able to include comparisons like those recited in steps (a) to (n) of claim 18.

Chou further teaches:

"*The time delay circuitry of FIG. 2 is responsive to the detector output pulses from detector 20 for producing delayed pulses each having a selected time delay relative to its detector pulse. Thus, the reoccurring bursts of energy supplied to the human body 10 for stimulating the body need not occur at precisely the same moment as the peak value in the heartbeat signal*" (page 10, lines 4-8 of Chou).

This seems to suggest that the operator of the electrotherapy apparatus of Chou can vary the delay of the burst of energy to stimulate a patient. However, as will become clear in the following, this delay is not readjusted for each heart beat, but it is fixed by the operator for the duration of the treatment once he has adapted the variable resistor on the electrotherapy apparatus of Chou. In contrast thereto, the processor recited in claim 18 of the present application readjusts the delay of the stimulation pulse for every heart beat, to ensure that the stimulation pulse is administered to the patient during every heart beat cycle at the same point

relative to the T-wave, irrespective of the changes of the heart rate. The position of the T-wave however changes as is best described by the Bazett relationship.

Further, Chou discloses:

"*The selected coarse delay pulse appearing at the output of OR gate 44 triggers the multivibrator 45 and the resulting fine delay pulse produced by multivibrator 45 appears on the multivibrator output line 48*" (page10, lines 24-26).

This confirms that the synchronization means of Chou does not include a processor, let alone that this processor is capable of calculating, determining and comparing the parameters of the heart rate detected using the ECG of the present application. Instead Chou uses static components such as the multivibrators mentioned above.

Chou additionally states:

"*As shown in FIG. 3, the delayed pulses on line 48 are supplied to a trigger input of a further monostable multivibrator 50. Each delayed pulse on line 48 triggers the multivibrator 50 to produce on the multivibrator output line 51 a pulse having the desired stimulation time duration. This time duration is determined by the resistance value of adjustable resistor 52 and the capacitance value of the capacitor 53 which are connected to the time constant inputs of the multivibrator 50. By adjustment of the resistor 52, this time duration can be varied over a range of 1 to 10 milliseconds or longer. Multivibrator 50 is triggered by the trailing edge of each delayed pulse appearing on the input line 48*" (page 11, lines 12-19).

The foregoing passage from Chou clearly demonstrates that the duration of stimulation of the apparatus of Chou is fixed for a treatment cycle and can only be adapted externally by an operator by varying the adjustable resistor 52, but there is again no automated process for carrying out an adjustment of the stimulation length, let alone that such an adjustment could be carried out using a processor. Moreover, the step above is not equivalent to step (i) of claim 18, and since the delay is fixed and the duration of stimulation is fixed for each treatment cycle by the operator of the apparatus of Chou, steps (j) to (n) of claim 18 are also not performed by the apparatus of Chou. Since there is no teaching or suggestion in Chou to automate the readjustment of the stimulation length or the delay time, there is no motivation for a person of

ordinary skill in the art to consider Chou, far less would Chou suggest or in any way motivate a person skilled in the art to use a processor in the manner recited in claim 18 to realize a much more sophisticated stimulation method.

Lastly, Chou teaches:

"*The time of occurrence of the trailing edges of the time duration control pulses of waveform 70 is determined by the RC time constant for the multivibrator 50 and, more particularly, by the setting of the resistance value of the adjustable resistor 52. As indicated in FIG. 5, the time of occurrence of this trailing edge is adjustable to provide the desired duration for the energy burst which is supplied to the stimulating mechanism*" (page14, lines 21-25).

This too demonstrates that no processor is used in Chou. Instead, static components are used which are set up at the beginning of a treatment cycle of a patient and do not vary during the treatment of that patient.

In conclusion, Chou does not disclose or suggest to one of ordinary skill in the art the use of a processor. Moreover, Chou does not disclose to carry out steps (b) to (n) of claim 18. As demonstrated above, Chou is only concerned with stimulating the patient rhythmically, but not in any defined manner.

Thus, Chou has not recognized and does not disclose or suggest to one of ordinary skill in the art that a reduction in heart load problems can be achieved by stimulating the heart in the counterpulsation mode, i.e. relative to the end of T-wave, as is evident from the fact that the synchronization mechanism of Chou does not include a processor which performs steps (a) to (n) of claim 18 and, separately therefrom, as further evidenced by the fact that Chou does not carry out steps (b) to (n) of claim 18.

Amended claim 18 is therefore not obvious in view of Chou.

Claims 19-24 and 38 are directed to specific features of the present invention which are patentable in their own right. These claims are further allowable because they depend from allowable parent claim 18.

CONCLUSION

In view of the foregoing, applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (415) 576-0200.

Respectfully submitted,

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